REMARKS

Claims 1-33 remain pending in the application. Amendments presented herein are believed to place the claims in a better form. All claims stand rejected on various grounds, as will be discussed below.

Completion of Priority Claim

As pointed out in the Office Action, applicants had not provided a certified copy of their priority application. Enclosed is a certified copy of India Patent Application 555/MAS/2002 filed on July 24, 2002. This submission should complete the remaining requirements for the priority claim under 35 U.S.C. § 119.

Rejection Under 35 U.S.C. § 112

Claim 1 was rejected under the second paragraph of the statute, for failing to recite a unit for measuring the hydrogen pressure. This has been corrected by inclusion of "atmospheres" following the numeric value. The rejection has been overcome and should not be maintained.

Rejection Under 35 U.S.C. § 102(e)

Claims 1, 2, 4-6, and 8-12 were rejected as being anticipated by teachings in U.S. Patent 6,649,765 to Vidyadhar et al.

In view of the priority for the present application dating from July 24, 2002, the Vidyadhar et al. patent (filed on February 12, 2003 and making no claim for an earlier priority date) is not prior art. Accordingly, the patent cannot anticipate the present claims and withdrawal of the rejection is appropriate.

First Rejection Under 35 U.S.C. § 103(a)

Claims 1, 2, 4-6, and 8-12 were rejected in paragraph 5 of the Office Action as being rendered obvious by a combination of teachings from the above-discussed Vidyadhar et al. patent and U.S. Patent 4,895,841 to Sugimoto et al.

Since the Vidyadhar et al. patent is not prior art, only the Sugimoto et al. patent remains to support the rejection. Sugimoto et al., as has been discussed in the applicants' specification, described a process for preparing cyclic amine compounds, including donepezil that was prepared by reacting 1-benzyl-4-piperidinecarboaldehyde with 5,6-dimethoxy-1-indanone, in the presence of n-butyllithium, to form 1-benzyl-4-[5,6-dimethoxy-1-indanon)-2-ylidenyl]methylpiperidine hydrochloride, then hydrogenating to obtain donepezil in a very low overall yield.

Direction for imposing obviousness rejections has been provided by M.P.E.P. § 706.02(j), as follows:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

As the Sugimoto et al. process is not related to the process that is being claimed by the applicants, and does not disclose or suggest all of the limitations of any claim, the rejection should not be maintained upon reconsideration.

Second Rejection Under 35 U.S.C. § 103(a)

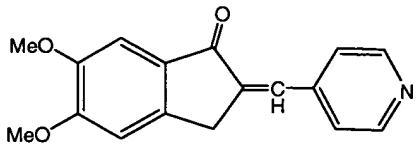
Claims 1, 2, 4-6, and 8-12 were rejected in paragraph 6 of the Office Action as being rendered obvious by the combination of patents described in the first rejection under this statute, the two patents further being combined with teachings from an article by H. Sugimoto et al. in *Bioorganic and Medicinal Chemistry Letters*, Vol. 2, No. 8, pages 871-876, 1992, and International Publication No. WO 97/22584.

As discussed above, the Vidyadhar et al. patent is not prior art, and therefore cannot be used in this rejection. Also as discussed above, the Sugimoto et al. patent has teachings related to a process different from that of the applicants' claims.

Therefore, unless the differences between the claims and the Sugimoto et al. patent teachings are supplied by the additional two documents, there can be no *prima facie* case for obviousness.

The Sugimoto et al. article discloses a preparation of compounds including donepezil, which is compound E2020 in Table 1 on page 872. The synthesis of all of the disclosed compounds appears to proceed according to Scheme I on page 872, and this scheme is very similar to the synthesis of donepezil that was taught by the Sugimoto et al. patent. As pointed out in the Office Action, hydrogenation in this scheme is accomplished using a 10% palladium carbon catalyst. However, nothing in the Sugimoto et al. article pertains to any of the other limitations of the rejected claims.

WO 97/22584 teaches a different process for preparing donepezil. However, this process does not involve a compound having the formula (IV):



(IV)

being the required starting material in all of the rejected claims. The document therefore cannot supply any of the limitations of the claims that are not shown by either of the Sugimoto et al. documents.

Since the combination of cited documents cannot provide sufficient information to meet or suggest all of the limitations of even claim 1, the rejection is not proper and should not be maintained upon reconsideration.

Third Rejection Under 35 U.S.C. § 103(a)

In paragraph 7 of the Office Action, claims 1, 2, 4-6, 8, 9, 11, and 12 were rejected as being rendered obvious by a combination of teachings from U.S. Patents 5,606,064 to Lensky and 4,895,841 to Sugimoto et al.

The Lensky patent teaches a process for preparing donepezil and related compounds. In the process for donepezil, 5,6-dimethoxy-2-(pyridin-4-yl)-methylene-indan-1-one (prepared in Example2) was reacted in Example 4 with benzyl bromide to

form 1-benzyl-4-(5,6-dimethoxyindan-1-on-2-ylidene)-methyl-pyridinium bromide, and this was hydrogenated using a platinum dioxide catalyst in Example 6 to form donepezil.

As was discussed above in connection with the first rejection under 35 U.S.C. § 103(a), the Sugimoto et al. patent prepared donepezil by reacting 1-benzyl-4-piperidinecarboaldehyde with 5,6-dimethoxy-1-indanone, in the presence of n-butyllithium, to form 1-benzyl-4-[5,6-dimethoxy-1-indanon)-2-ylidenyl]methylpiperidine hydrochloride, then hydrogenating.

No combination of teachings from these two patents will provide a *prima facie* case for obviousness of the rejected claims. Neither of the disclosed processes proceeds according to the applicants' claims, and the processes of the patents are too divergent to form any meaningful combination. One cannot simply substitute a particular reaction involving one compound, for another reaction involving a quite different compound. Moreover, even if such substitution of process steps is made in the processes of the cited patents, the result will not equal the applicants' claimed process.

Considered in view of the directive from M.P.E.P. §706.02(j), this rejection is not proper and should not be maintained.

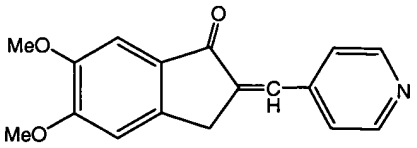
Fourth Rejection Under 35 U.S.C. § 103(a)

In paragraph 8 of the Office Action, claims 1, 2, 4-6, 8, 9, 11, and 12 were rejected as being unpatentably obvious over the combination of U.S. Patents 5,606,064 to Lensky and 4,895,841 to Sugimoto et al., with the Sugimoto et al. article in *Bioorganic and Medicinal Chemistry Letters*. Deficiencies of the combined teachings from the two patents was discussed immediately above.

The addition of teachings from the Sugimoto et al. article does not assist in meeting the limitations of the rejected claims. The process description in this article is deficient in its detail: one cannot determine what group was present as "R_4" in each synthesis of the described process. Since the process presumably was used to prepare all of the different described compounds, the particular R_4 that was present when E2020 was made is not apparent. There also is no information about conditions that were used to prepare each of the various compounds. Contrary to the implication in the rejection, Table 3 on page 873 of the article has nothing to do with the synthesis

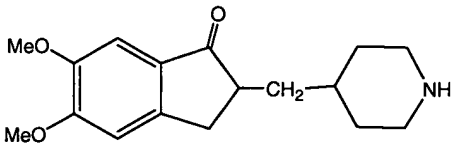
description, but simply reports varying biologic activity results for a number of compounds.

Using the applicants' claim 1 as an example, there is no teaching in the combined cited documents relating to hydrogenating an alcohol suspension of a palladium metal on a support carrier and the compound of Formula (IV):



(IV)

under the claim-required conditions, isolating the compound having Formula (VI):



(VI)

and converting that compound to donepezil. This rejection is not proper, and should now be withdrawn.

Fifth Rejection Under 35 U.S.C. § 103(a)

All of claims 1-33 were rejected under this statute in paragraph 9 of the Office Action, as being obvious over the combination of U.S. Patents 5,606,064 to Lensky and 4,895,841 to Sugimoto et al., with the Sugimoto et al. article in *Bioorganic and Medicinal Chemistry Letters* and WO 97/22584.

The discussion above, regarding the fourth obviousness rejection, fully applies to this rejection. The additional cited document does not add anything that would overcome the noted deficiencies of the above-discussed combination. WO 97/22584 teaches a very different process from that of Lensky and that of Sugimoto et al.; the statement in the Office Action that the respective processes are "analogous" is simply not correct. The process of WO 97/22584 for preparing donepezil does not involve any of the intermediates of any other cited document, or any intermediate of the applicants' claimed process, prior to the formation of the applicants' compound having Formula (VI).

This combination of documents does not contain or suggest all of the applicants' claim limitations, and the rejection is not proper. Withdrawal upon reconsideration is respectfully requested.

CONCLUSION

Entry of the present amendments, consideration of the foregoing discussion, and allowance of the pending claims are now appropriate. If any minor matters remain to be resolved before disposition of the application, please contact the undersigned to arrange for a telephonic or personal interview.

Respectfully submitted,

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